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L. ZIEVE

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EFFECT OF BENZEDRINE ON ACTIVITY*

L. ZIEVE
University of Minnesota

Casual observation of the immediate after-effects of benzedrine on the human organism indicates a definite hyperkinesis. Greater excitability and a lowered threshold of stimulation are evident. Clinical studies find that benzedrine has a stimulating action on the higher nervous centers; also that it produces a hypertension in the blood vessels. Use is made of its kinetic effect in the treatment of narcoleptic cases (1, 2). Studies of the comparative stimulating effects of various drugs and hormones on the rate of establishment and extinction of a conditioned response illustrate the activating effect of benzedrine (3, 4). The conditioned response was the pressing of a lever. During periodic re-conditioning benzedrine caused an increase of 130 per cent in the rate of responding, and was in this respect unusually effective. It also caused a marked increase in the rate of responding during extinction, being more effective than caffeine.

None of these studies measured spontaneous activity itself. The need for a direct quantitative measurement of the increase in spontaneous activity as a result of ingesting benzedrine prompted this experiment.

The method consisted in running twenty-four three-month-old albino rats in revolving activity drums. These cages have been shown to be reliable (5). The animals were run for three successive 15-day periods, the first and third periods being controls during which no benzedrine was given. An interval of three days was allowed between the second and third periods during which no records were taken though the animals remained in the cages. Each day during the second period 2 cc. of a benzedrine solution were thoroughly mixed with the food. Addition of the drug was made separately to the individual food cups to assure accurate dispension. The dose amounted to 2 mgm. of benzedrine per kilo of body weight. This amount was chosen as a medium dose for animals weighing about

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250 gms., after preliminary experimentation with doses varying from .5 mgm. to 40 mgm. per kilo of body weight.[1] The amount of food eaten by the animals was held constant from day to day.

Means were calculated in terms of revolutions of an 8-in. revolving cage for the first control, C_1, the test run, T, and the second control, C_2. The results are summarized in Table I.

TABLE I

REVOLUTIONS OF CAGES IN CONTROL (C_1, C_2) AND BENZEDRINE (T) PERIODS

Period	Mean	σ	D/σ_D	$\frac{\sigma}{\text{Mean}}$
C_1	62,500	51,900	C_1-T: 3.54	83.04%
T	135,000	85,950	C_2-T: 3.05	63.67%
C_2	70,840	56,840	C_1-C_2: 0.53	80.24%

It will be noted that between the first control and the test run there is a critical ratio of 3.54, between the second control and the test run a critical ratio of 3.05, and between the first and second controls a critical ratio of 0.53. The great differences between C_1 and the test run and between C_2 and the test run leave little room for doubt as to the hyperkinetic effect of benzedrine. An increase of more than 100 per cent over the average control activity is produced. These differences are especially significant in view of the fact that only 24 animals were used.

The ratio of 0.53 between C_1 and C_2 represents an important isolating control showing that the increase in activity during the test run was not the result of prolonged stay in the activity cages.

A difference of approximately 20 per cent between the coefficients of variation for the two control periods and the test period brings out a further result; namely, that benzedrine tends to reduce relative variability. The decrease in relative variability resulted from a proportionately greater increase in activity of the less active animals. In other words, benzedrine seems to have the greatest activating effect on the least active animals.

Taking the activity increase as a measure of the physiological effects of benzedrine, one can get some evidence as to the tolerance built up to the drug by dividing the test run, which consisted of records for fifteen consecutive days, into 3 equal sub-periods and comparing the records for each sub-period. Means computed for these sub-periods are given in Table II.

[1] The experimentation on varying doses was largely the work of Mr. H. Crook.

TABLE II

REVOLUTIONS OF CAGES DURING SUCCESSIVE PARTS OF THE BENZEDRINE PERIOD

Five-day Sub-periods	Mean	σ	$\frac{\sigma}{\text{Mean}}$
First	36,667	23,570	64.28%
Second	42,917	29,577	68.92%
Third	48,333	35,668	73.80%

It would be expected that with the development of tolerance to the drug there would be a decrease in activity unless the dosage is very near the depressant stage, which is unlikely. Comparison of the records in Table II of the three sub-periods indicates no decrease, but rather a slight though insignificant increase. It is, therefore, probable that the animal does not build up a tolerance to the drug.

In the light of the following data, there seems to be little likelihood that an effect of the dose beyond 24 hours needs to be considered here. The mean number of revolutions for the last day of the benzedrine period was 11,250, for the following day with no benzedrine 3,167, and for the first day of the second control period 3,917.[2] The respective sigmas were 8,319, 2,779, and 3,226. Such a sudden decrease, notwithstanding the large standard deviations, stands in contradistinction to the fairly gradually descending curve that one would expect had there been a cumulative effect.

In Table II are listed coefficients of variation that appear to have uniformly increasing values. This seemingly significant orderliness is probably an artifact resulting from the arbitrary method of dividing the test period into sub-periods. When the test period was broken up into three-day intervals so that there were five sub-periods instead of three, the coefficients of variation showed a chance distribution. Thus the coefficients for the first, second, third, fourth, and fifth sub-periods were respectively 71.50, 61.82, 66.62, 72.63, and 69.81 per cent.

Incidental observations on the effects of large doses of benzedrine (40 mgm. per kiloweight) on activity indicate that it has a depressant effect. It was difficult to get very accurate records because interfering visceral inhibitory and sudorific effects were marked.

[2] The second control began on the fourth day following the test period. During the intervening time the animals remained in the cages.

Summary

Records of the spontaneous activity of animals were accumulated over a period of 15 days during which a medium dose of benzedrine was ingested daily. These records were compared with similar records of two control periods of the same length, one preceding and one following the benzedrine test period. The significant differences between the control and test periods definitely illustrate the activating properties of benzedrine. A difference of approximately 20 per cent between the relative variability of the control periods and the test period indicates that benzedrine tends to reduce relative variability. Evidence obtained indicated the probability that no tolerance was built up to the drug.

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